

**REMARKS**

**Formal Matters**

Applicants have amended claims 10 and 15. Applicants have canceled claim 14, without prejudice or disclaimer, and have added new claims 19-24. No new matter has been added by way of these new claims. Support for the new claims can be found in the specification as originally filed at, for instance, original claims 2, 3, and 9, and page 8, line 29 to page 9, line 13.

Claims 10-13, 15, and 19-24 are currently pending.

**Information Disclosure Statement**

Applicants note that the Office did not consider the *Fass* reference ("Factor VIII Structure and Function," Ann. N.Y. Acad. Sci., 614:76-88 (1991)) listed on page 2 of the Information Disclosure Statement submitted September 26, 2003. Applicants have enclosed another copy of the Form 1449 with this response and respectfully request that the Office indicate that it has considered this reference.

**Written Description Rejection**

The Office rejected claims 10-15, as failing to comply with the written description requirement. See Office Action at page 2. Specifically, the Office alleged that claims 10-14 lack written description because they recite "any amino acid" and/or "any alkali metal." See Office Action at page 3. Applicants note that claim 14 is canceled and therefore the rejection of this claim is moot. Applicants respectfully submit that one of skill in the art would recognize that the inventors had possession of the claimed

invention at the time of filing based on the terms “alkali metals,” “alkali earth metals,” and “amino acid.” The alkali metals consist of the compounds of Group IA on the periodic table (H, Li, Na, K, Rb, Cs, Fr) and the alkaline earth metals consist of the compounds of Group 2A on the periodic table (Be, Mg, Ca, Sr, Ba, Ra). The group of metals envisioned by Applicants is well-defined. The term “amino acid” is also a well-known term. Further, Applicants describe amino acids that can be used in the invention as “other physiological or even nonphysiological amino acids, such as  $\alpha$ -alanine,  $\alpha$ -,  $\beta$ -, or  $\gamma$ -aminobutyric acid, lysine, valine, asparagine and glutamic acid.” Specification, sentence spanning pages 7-8. The terms “alkali metals,” “alkali earth metals,” and “amino acid” convey with sufficient detail to one skilled in the art what was in Applicants’ possession at the time of filing. Furthermore, Applicants describe actual reduction to practices of the invention in the “Examples” section of the specification at, for instance, pages 9-11. Example 1 demonstrates the fractional precipitation of a vWF/FVIII:C concentrate using glycine (amino acid) and NaCl (alkali metal salt). The specification “describes the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.” M.P.E.P. § 2163, subpart I. Applicants therefore respectfully request that the Office withdraw the written description rejection of claims 10-13.

The Office specifically rejected claim 15 because the claim “does not refer to any physical and chemical conditions for the stabilization and pasteurization of the concentrate or the concentrate precursor.” Office Action at page 3. Applicants respectfully traverse. Applicants have amended claim 15 to place it in proper U.S.

format for a method claim. Applicants respectfully submit that one of skill in the art would recognize that the inventors had possession of the claimed invention at the time of filing. Pasteurization is defined as “partial sterilization of a substance esp. a liquid (as milk) at a temperature and for a period of exposure that destroys objectionable organisms without major chemical alteration of the substance.” Merriam-Webster’s Collegiate Dictionary 848 (F.C. Mish ed., 10<sup>th</sup> ed. 2001). Applicants describe an actual reduction to practice of “pasteurization” in Example 1 of the specification at page 10, line 3. Applicants also describe an actual reduction to practice of “stabilizing” in Example 1 of the specification at page 10, lines 1-2. The specification discusses stabilization at, for instance, page 8, lines 38-39, stating that the liquid can “be stabilized, for which purpose calcium ions are particularly suitable.” The terms “pasteurizing” and “stabilizing” convey with sufficient detail to one skilled in the art what was in Applicants’ possession at the time of filing. Therefore, Applicants respectfully request that the Office withdraw the written description rejection of claim 15.

### **Enablement Rejection**

The Office rejected claims 10-15, because allegedly the specification does “not reasonably provide enablement for all amino acids and all metal salts.” Office Action at page 3. Applicants respectfully traverse. As noted above, claim 14 is canceled and therefore the rejection of this claim is moot. Applicants respectfully note that claims 10-13 and 15 are not directed to “all metal salts,” but “at least one of an *alkali* metal and an *alkaline earth* metal salt.” One of skill in the art would be able to make and use the claimed invention using the following teachings in the application as a guide:

- Choice and preparation of starting material is described on pages 6-7 of the specification.
- The specification at pages 7-9 teaches how to obtain the concentrate of the invention by precipitation, including particular concentration ranges of precipitants.
- Example 1 (specification at pages 9-11) teaches fractional precipitation of the vWF/FVIII:C concentrate. Example 1 also teaches analysis of the precipitates for vWF:RCoF activity, which measures the functional activity of vWF, as well as measurement of vWF:Ag and FVIII:C concentrations.
- Example 2 (specification at pages 11-14) teaches a first and a second precipitation, each precipitation followed by a measurement of vWF activity.
- Example 3 (specification at pages 14-16) teaches precipitation of the vWF/FVIII:C fraction with the same NaCl/glycine concentration, but with varying addition and incubation times.
- Example 4 (specification at pages 16-18) teaches fractional precipitation of the vWF/FVII:C concentrate and, at the same time, teaches a first and second precipitation.
- Example 5 (specification at pages 18-21) teaches stabilization, sterilization, and lyophilization of a fraction enriched with high molecular weight vWF multimers. Example 5 also teaches the production of a vWF/FVIII:C concentrate in which the vWF high molecular weight markers were reduced.

- Example 6 (specification at page 22) demonstrates fractional precipitation of high molecular weight vWF multimers from a supernatant containing recombinant FVIII:C and plasma vWF.

One of skill in the art based on these teachings would be able to both make and use the factor VII:C-containing von Willebrand factor concentrate. The amino acid and alkali metal or alkaline earth metal salt can be easily tested to select the conditions that result in an increased content of functional, high molecular weight vWF multimers. No undue experimentation is required. Therefore, Applicants respectfully request that the Office withdraw the enablement rejection of claims 10-13 and 15.

#### **Indefiniteness Rejections**

The Office rejected claims 10-15 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. See Office Action at page 6. Specifically, the Office stated that in claim 10, the full names of “vWF:RcoF” and “vWF:Ag” must be spelled out. *Id.* Applicants have replaced these abbreviations in claim 10 with the full names. Therefore, Applicants respectfully request that the Office withdraw this rejection of claim 10.

The Office also rejected claim 10 because allegedly the max value for the ratio “greater than 1” is not clear. *Id.* Section 2173.05(b) of the M.P.E.P. states that “[a]cceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification.” Applicants respectfully submit that no ambiguity is created with regard to the “greater than 1” limitation. One of

ordinary skill in the art would understand that the vWF:RcoF activity must simply be greater than the vWF antigen concentration. Section 2173.05(b) of the M.P.E.P. also states that the “fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph.” Merely because no maximum is given for the ratio of vWF:RcoF activity to vWF:Ag, does not mean that in light of the specification, one of ordinary skill in the art would not understand what is being claimed. The ratio is simply calculated as an indicator of vWF activity, based on the total amount (either active or inactive) of vWF present. Based on these arguments, Applicants respectfully request that the Office withdraw the indefiniteness rejection of claim 10.

The Office rejected claim 14 because allegedly the terms “preferential precipitation” at “lower concentrations” or “higher concentrations” are indefinite. See Office Action at page 6. Applicants respectfully note that claim 14 has been canceled, without prejudice or disclaimer. Therefore, these indefiniteness rejections are moot.

The Office rejected claim 15 because allegedly the term “concentrate precursor” is indefinite. Specifically, the Office asserts that the term is indefinite because “the structure or name of the precursor is not provided in the claim, and the claim lacks antecedent basis to claim 10.” Office Action at page 6. Applicants have replaced the phrase “concentrate precursor product” in claim 15 with “precursor product.” Section 2173.05(b) of the M.P.E.P. states that “[a]cceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification.” Applicants respectfully assert that one of ordinary skill in the art would

understand that the claims are directed to a “process for producing a concentrate.”

Therefore, a “precursor product” is any substance that precedes the final formation of the concentrate. The term “precursor” is defined in one dictionary as “a substance, cell, or cellular component from which another substance, cell, or cellular component is formed.” Merriam-Webster’s Collegiate Dictionary 915 (F.C. Mish ed., 10<sup>th</sup> ed. 2001). One of ordinary skill in the art would understand that stabilization or pasteurization of the liquid can occur at any time before the final concentrate is produced.

In addition, “the failure to provide explicit antecedent basis for terms does not always render a term indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite.” M.P.E.P. § 2173.05(e). Applicants respectfully submit that one of skill in the art would understand what is claimed, as described above. Furthermore, the full phrase in claim 15 “or a precursor product produced during said process” refers back to the entire process of claim 10 and precursors to the concentrate produced therein. Based on these arguments, Applicants request that the indefiniteness rejection of claim 15 be withdrawn.

**CONCLUSION**

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

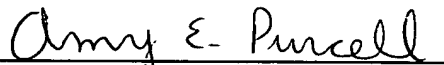
Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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By

  
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